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The Incidence of Basal Cell Carcinoma in Croatia: An Epidemiological Study

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SUMMARY The aim of the study was to investigate the basal cell carcinoma (BCC) incidence in Croatia in the 2003-2005 period. Data were collected from University Department of Dermatology and Venereology, Zagreb University Hospital Center and National Cancer Registry. The age-specific incidence rate and age-standardized incidence rate were calculated *per* 100,000 inhabitants according to the latest population census in Croatia from 2001. In the study period, there were 7,244 BCC cases (3,519 men and 3,725 women) in Croatia. The crude incidence rate for the Croatian population of 100,000 was 54.9 for men and 53.9 for women. The age-standardized incidence rate (adjusted for the world standard population) was 33.6 for men and 24.5 for women. The head and neck were almost exclusive localizations of BCC. The highest BCC incidence was recorded in Zadar County. The incidence of BCC was high in both littoral and inland counties of Croatia. Study results will serve as reference figures on studying the trend of BCC incidence in Croatia and Europe in the forthcoming years.

KEY WORDS: basal cell carcinoma, incidence, epidemiology, Croatia

INTRODUCTION

Basal cell carcinoma (BCC) is the most common cancer in humans (1). The tumor usually arises from the lowermost layers of the epidermis, although a small percentage may originate from the outer root sheath of the pilosebaceous unit (2). It typically occurs in the areas of chronic sun exposure (1). BCC is usually slow growing and rarely metastasizes, but it can cause clinically significant local destruction and disfigurement if neglected or inappropriately treated (3). Men are affected slightly more often than women (1). The male to female ratio is approximately 3:2 (3). The world population-based data for skin cancers show that the skin cancer incidence has been increasing in the last years all over the world (4,5). The rising incidence rates of BCC have probably been caused

Acta Dermatovenerol Croat
2009;17(2):108-112

by a combination of increased sun exposure or exposure to ultraviolet light (UVL), increased outdoor activities, changes in clothing style, increased longevity, ozone depletion, genetics and in some cases immune suppression (6). Light hair and eye color, and inability to tan are also risk factors for the development of BCC (1,6). The major environmental cause of BCC is exposure to solar ultraviolet radiation (1). It causes mutations in cellular DNA which, when unrepaired, lead to the unrestrained growth and tumor formation, and also act as an immunosuppressant to prevent tumor rejection (7,8).

The Republic of Croatia is situated in the southeast of Europe and is divided into 3 geographical regions: The Mediterranean, mountainous and the Pannonian region (9). The importance of the geographical location of Croatia is increased by the Adriatic Sea, with its coast and islands with approximately 2,600 hours of sunshine *per* year are one of the sunniest on the Mediterranean (9). Territorially and politically, Croatia is divided into 20 counties, of which the Istria, Split-Dalmatia, Zadar, Šibenik-Knin, Dubrovnik-Neretva Counties, and parts of the Primorje-Gorski kotar and Lika-Senj Counties are situated on the Adriatic Sea (9). The BCC incidence in Croatia was not reported until 2003. Upon the initiative of the Committee of Dermatology and Venereology, Ministry of Health and Social Welfare, Republic of Croatia, since January 2003, the incidence of BCC has been monitored and studied at University Department of Dermatology and Venereology, Zagreb University Hospital Center and National Cancer Registry.

The aim of the present study was to assess the incidence of BCC in Croatia during the 2003-2005 period.

PATIENTS AND METHODS

We studied 7,244 cases of BCC (3,519 men and 3,725 women) diagnosed in Croatia between January 1, 2003 and December 31, 2005. Data were collected by use of a structured questionnaire designed by the Committee of Dermatology and Venereology of the Ministry of Health and Social Welfare of Croatia. The questionnaire contained information on BCC cases diagnosed at dermatology departments throughout Croatia and reported to the University Department of Dermatology and Venereology, Zagreb University Hospital Center. Data were also derived from hospital discharge notification called “Onco Type Cards” and outpatient “Malignant Neoplasm Notification”, submitted to the National Cancer Registry. All BCC cases were verified by histopathology. Data were encoded according to the International Classification of Diseases Tenth Revision (ICD-10), i.e. code C44 (10). The patients treated in Croatia but living abroad and those with recurrent tumors were excluded from data analysis. Data on the date of diagnosis, patient age and sex, permanent address, BCC localization and histopathologic report were recorded. In the total number of BCC cases, the tumor localization was unknown in 361 male and 388 female patients. Patient age was unknown in 103 male and 128 female BCC patients. Age-specific incidence rate (mean *per* year) was calculated *per* 100,000 inhabitants according to the latest population census in Croatia from 2001 (11). In order to allow comparison among Croatian counties and with the world, we used age-standardized incidence rates.

Statistical analysis was done by use of SPSS 13.0 software.

RESULTS

The total number of BCC was 7,244, including 3,519 men and 3,725 women, yielding a male to female ratio of 0.9. Anatomical distribution of BCC is shown in Tables 1 and 2. The most common lo-

Table 1. Distribution (number of cases, %) of basal cell carcinoma in the head and neck region in Croatia 2003-2005

	Men	Women
Eyelid, unspecified	54 (2)	65 (2)
Lower eyelid	58 (2)	71 (2)
Upper eyelid	18 (1)	40 (1)
Medial ocular canthus	51 (2)	60 (2)
Lateral ocular canthus	4 (0.1)	5 (0.1)
Nose	490 (16)	645 (19)
Lips, unspecified	16 (1)	21 (1)
Lower lip	9 (0.3)	21 (1)
Upper lip	16 (1)	34 (1)
Chin	15 (1)	20 (1)
Cheeks	713 (23)	884 (26)
Forehead	347 (11)	360 (11)
Scalp	79 (3)	67 (2)
Ears	173 (5)	106 (3)
Preauricular region	64 (2)	32 (1)
Retroauricular region	49 (2)	34 (1)
Neck	124 (4)	102 (3)
Total	2280 (72)	2567 (77)

The percentage of the total number of basal cell carcinoma in the known localization in men and women; known localization (men/women 3,158/3,337); unknown localization (men/women 361/388)

Table 2. Distribution (No. of cases, %) of basal cell carcinoma on the trunk and extremities in Croatia, 2003-2005

	Men	Women
Trunk, unspecified	137 (4)	72 (2)
Back	334 (11)	336 (10)
Chest	116 (4)	74 (2)
Abdomen	21 (1)	69 (2)
Upper arm	139 (4)	72 (2)
Forearm	30 (1)	14 (0.4)
Hand	11 (0.3)	6 (0.1)
Upper leg	17 (1)	39 (1)
Calve	65 (2)	67 (2)
Foot	4 (0.1)	9 (0.2)
Buttocks	4 (0.1)	7 (0.2)
Vulva	0	5 (0.1)
Total	878 (28)	770 (23)

The percentage of the total number of basal cell carcinoma in the known localization in men and women; known localization (men/women 3158/3337); unknown localization (men/women 361/388)

calization of BCC was on the head and neck (72% in men and 77% in women) in comparison with the trunk and extremities (28% in men and 23% in women). The cheeks were an almost exclusive localization of BCC in both sexes (23% in men 26% in women), followed by the nose (16% in men and 19% in women) and forehead (11% in both sexes). Of non-photoexposed skin areas, a high percentage of cases were found on the back (11% in men and 10% in women). The ratio of photoexposed (head, neck and hand) to non-photoexposed skin areas was 3:1. The age-specific incidence rate of BCC and the adjusted rates for the world standard population are listed in Table 3. The highest increase in BCC incidence was after age 60, with a peak after age 80 in both sexes. The incidence

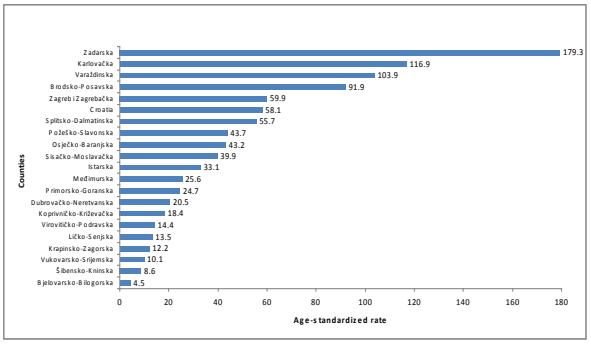

Figure 1. The age-standardized rate of basal cell carcinoma in men in Croatian counties 2003-2005

of BCC according to Croatian counties is shown in Figures 1 and 2. The highest incidence was recorded in Zadar County and lowest incidence in Bjelovar-Bilogora County (Figs. 1 and 2).

DISCUSSION

Before this study, there were no published data on the incidence of BCC in Croatia. In our opinion, the exact BCC incidence is not known because different specialists are involved in the diagnosis and treatment of BCC but fail to report it, thus making respective data collection more difficult. BCC is generally a tumor of Caucasians, especially those with fair skin (1). It is rare in dark-skinned individuals (12). The tumor characteristically develops on the sun-exposed skin, with 30% occurring on the nose (13). The greatest percentage of cases in our study were localized on the cheeks (49%), followed by the nose (35%) and forehead (22%). Twenty-one percent of BCC cases were recorded on the back as a non-photoexposed skin area. It may suggest that several months or years of intense UVL exposure during holidays or agricul-

Table 3. The incidence rate of basal cell carcinoma (BCC) in Croatia, 2003-2005

Age group (yrs)	Total number of BCC (male/female)	Age-specific incidence rate* (male/female)	Age-standardized incidence rate (world)† (male/female)
0-9	0/0	0/0	0/0
10-19	3/0	0.3/0	0.05/0
20-29	4/20	0.4/2.3	0.06/0.36
30-39	34/63	3.7/6.9	0.44/0.82
40-49	145/161	14.4/16.2	1.72/1.94
50-59	401/393	52.0/48.0	4.68/4.32
60-69	961/901	138.6/105.8	9.70/7.40
70-79	1308/1364	345.9/211.4	10.37/6.34
80+	560/695	652.3/326.8	6.52/3.26
Total	3416/3597	54.9/53.9	33.6/24.5

*Mean annual incidence rate *per* 100,000 inhabitants (Croatian population census 2001); †incidence rate *per* 100,000 inhabitants (world standard population 1980); unknown age (men/women 103/128)

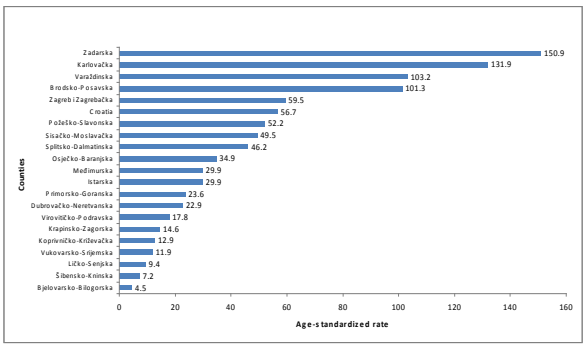

Figure 2. The age-standardized rate of basal cell carcinoma in women in Croatian counties 2003-2005

tural work may have deleterious long-term effects (1). Men are affected more than women, with male to female ratio being approximately 3:2 (3); in our study it was 0.9. The possible explanation was that women were more sun exposed to solar UVL and tanning beds in order to get darker skin complexion. Another reason could be the higher number of live women aged >50 in Croatia (11). The longer population life expectancy increases the rate of BCC in the elderly (1). In our study, the youngest age group with the diagnosis of BCC were male patients aged 10-19. There were no data available to show the possible presence of genodermatoses in these cases, where BCC occurs in early childhood.

Analysis of the age-standardized incidence rate according to counties revealed the highest BCC incidence in Zadar County (179.3 for men and 150.9 for women). We expected a high incidence of BCC in other counties of Mediterranean Croatia; however, the results were different from what we expected. The Karlovac County (116.9 for men and 131.9 for women) and Varaždin County (103.9 for men and 131.9 for women), situated in inland Croatia, had the highest BCC incidence as compared with littoral counties except for Zadar County (Figs. 1 and 2). The Šibenik and Knin Counties, territorially closest to the Zadar County, had a low BCC incidence (8.6 for men and 7.2 for women). It remains questionable whether such a result is credible, or the patient reports were incomplete. We also tried to explain these results by the share of agricultural population in the counties with high BCC incidence. According to the latest agricultural registry from 2003, Karlovac County had 19,171, Varaždin County 33,451, Brod-Posavina County 20,704, the City of Zagreb and Zagreb County 52,404, and Zadar County 14,392 agricultural households (14). Therefore, the possible reason for the higher

Table 4. The age-standardized incidence rate of basal cell carcinoma in Mediterranean countries

	Male	Female
Malta	53.4	32.8
Italy,Genoa Province	50.0	34.6
Italy, Veneto Region	55.3	38.6
Italy, Varese Province	48.3	30.9
Croatia	33.6	24.5
Spain, Murcia	36.3	24.9
Slovenia	32.6	24.9
Italy, Naples	13.6	8.3
Turkey, Antalya	13.7	11.9
Tunisia, Centre, Sousse	9.5	8.6
Algeria, Setif	4.4	2.6
Egypt, Gharbiah	3.5	1.5
Israel	1.3	1.8
Portugal, Porto	0.1	0.3

Source: Cancer Incidence in Five Continents, Vol IX, IARC (1998-2000), except for Croatia

BCC incidence in inland counties may have been intermittent but the intensive sun exposure during agricultural work. The increased migration of the population during the war in Croatia 1991-1995 was another potential factor that may have influenced BCC occurrence in the counties with higher BCC incidence. The highest number of population had migrated from the Vukovar-Srijem County to different areas of Croatia, which could explain the low incidence of BCC in this county (10.1 for men and 11.9 for women). Another factor that could have indirectly influenced the increased incidence of BCC in inland Croatia was the migration of the population from the Mediterranean Croatia to the inland regions for educational and economic reasons. This means that the population born in the Mediterranean Croatia in the early childhood lived in the area of higher insolation. An intensive UVL exposure in childhood and adolescence caused the development of BCC later in life (6).

International Agency for the Research of Cancer (IARC) issues the publications Cancer Incidence in Five Continents every five years (4,5). The last edition presents information on skin cancers in the period from 1998 to 2002 (5). To date, Croatia has not reported data on the incidence of BCC to IARC. Comparison of our data with data on other countries registered in IARC showed the age-standardized incidence rates in Croatia (33.6 men and 24.5 women) to be comparable to Slovenia (32.6 men and 24.9 women) and Italy, Parma Province (33.3 men and 22.9 women) (5). The highest rates were recorded in Brazil, Goiania

Acta Dermatovenerol Croat
2009;17(2):108-112

(149.0 men and 137.0 women), and in Europe in Switzerland, Geneva (100.0 men and 93.0 women) (5). Table 3 shows the age-standardized incidence rates of BCC in Mediterranean countries.

Among the factors influencing the etiology of BCC, it is necessary to arouse the people's awareness of the importance of sun protection. The message of UVL protection should include the triad of wearing protective clothing (15), avoiding the midday sun when the UVL intensity is greatest, and regular use of sunscreen (full range of UVL protection) to have the greatest impact in lowering skin cancer risk (16). This prevention should also include follow up for all patients with a history of BCC. It is especially important because these patients have a threefold risk of melanoma and by 36%-50% higher risk of developing a second primary BCC (1). Individuals with a personal history of BCC have an increased risk of subsequent non-cutaneous malignancies (17).

We emphasize the importance of regular reports of BCC cases, as it is the only way to collect complete data for monitoring the trend in the incidence of BCC in Croatia and Europe in the forthcoming years.

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